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10/019,740	05/08/2002	Nancy Cauwenberghs	INL-091	7478
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Kirkpatrick & Lockhart Preston Gates Ellis LLP			JUNG, UNSU	
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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	Application No.	Applicant(s)	
	10/019,740	CAUWENBERGHS ET AL.	
	Examiner Unsu Jung	Art Unit 1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) Responsive to communication(s) filed on 22 February 2007.
- 2a) This action is FINAL.                            2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) Claim(s) 31-41 and 46-62 is/are pending in the application.
  - 4a) Of the above claim(s) 46 and 47 is/are withdrawn from consideration.
- 5) Claim(s) \_\_\_\_\_ is/are allowed.
- 6) Claim(s) 31-41 and 48-62 is/are rejected.
- 7) Claim(s) \_\_\_\_\_ is/are objected to.
- 8) Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on 18 January 2006 is/are: a) accepted or b) objected to by the Examiner.
 

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
  - a) All    b) Some \* c) None of:
    1. Certified copies of the priority documents have been received.
    2. Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
    3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- 1) Notice of References Cited (PTO-892).
- 2) Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) Information Disclosure Statement(s) (PTO/SB/08)  
Paper No(s)/Mail Date \_\_\_\_\_.
- 4) Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_\_.
- 5) Notice of Informal Patent Application
- 6) Other: \_\_\_\_\_.

**DETAILED ACTION**

***Continued Examination Under 37 CFR 1.114***

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on February 22, 2007 has been entered.

***Response to Amendment***

2. Applicant's declaration under 37 C.F.R § 1.132 in the reply filed on February 22, 2007 have been acknowledged and entered.

3. Applicants' amendments to add new claim 62 and amend claims 31, 32, 37, 38, and 40 in the reply filed on February 22, 2007 have been acknowledged and entered.

4. Claims 31-41 and 46-62 are pending, claims 46 and 47 have been withdrawn from consideration, and claims 31-41 and 48-62 are under consideration for their merits.

***Rejections Withdrawn***

5. Applicant's arguments, see pp5-12, filed on February 22, 2007, with respect to the rejection under 35 U.S.C. 103(a) as being unpatentable over Favaloro et al. (*Pathology*, 1993, Vol. 25, pp152-158) in view of Christophe et al. (*Blood*, 1994, Vol. 83, pp3553-3561), and Handin (U.S. Patent No. 5,321,127, June 14, 1994) have been fully considered and are persuasive. The rejection of claims 31, 40, 41, 48-50, and 60 under 35 U.S.C. 103(a) as being unpatentable over Favaloro et al. in view of Christophe et al., and Handin has been withdrawn. Subsequently, the following rejection have also been withdrawn:

- Rejection of claims 55 under 35 U.S.C. 103(a) as being unpatentable over Favaloro et al..in view of Christophe et al., and Handin, and further in view of Solen et al. (U.S. Patent No. 6,043,871, Filed Mar. 3, 1997).

6. Applicant's arguments, see pp5-12, filed on February 22, 2007, with respect to the rejection under 35 U.S.C. 103(a) as being unpatentable over Favaloro et al. in view of Christophe et al., Hoylaerts et al. (*Biochem. J.*, 1995, Vol. 386, pp453-463), and Handin have been fully considered and are persuasive. The rejection of claims 31-39, 41, 48-53, and 56-60 under 35 U.S.C. 103(a) as being unpatentable over Favaloro et al. in view of Christophe et al., Hoylaerts et al., and Handin has been withdrawn. Subsequently, the following rejection have also been withdrawn:

Art Unit: 1641

- Rejection of claims 54 under 35 U.S.C. 103(a) as being unpatentable over Favaloro et al. in view of Christophe et al., Hoylaerts et al., and Handin as applied to claim 53 above, and further in view of Batz et al.; and
- Rejection of claim 61 under 35 U.S.C. 103(a) as being unpatentable over Favaloro et al. in view of Christophe et al., Hoylaerts et al., and Handin in light of Vicente.

***Claim Rejections - 35 USC § 103***

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

8. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

9. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of

the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

10. Claims 31-41, 48-53, 56-60, and 62 are rejected under 35 U.S.C. 103(a) as being unpatentable over Favaloro et al. (*Pathology*, 1993, Vol. 25, pp152-158) in view of Vischer et al. (*Critical Reviews in Oncology/Hematology*, Apr. 1999, Vol. 30, pp93-109), Hoylaerts et al. (*Biochem. J.*, 1995, Vol. 386, pp453-463), and Handin (U.S. Patent No. 5,321,127, June 14, 1994).

Favaloro et al. teaches a method for detecting von-Willebrand disease (vWD) comprising the steps of (see entire document, particularly Abstract):

- a) detecting von-Willebrand factor (vWF) activity in a sample (p153, right column, *Collagen binding assay for vWF*);
- b) determining the amount of vWF-antigen in the sample (p153, left column, *ELISA assay for vWF:Ag*);
- c) determining the ratio between vWF-activity and vWF-antigen for the sample (Abstract);
- d) comparing the ratio obtained under c) to a range of ratios established as normal range (p154, Table 1);

e) detecting vWD based on the comparison result obtained under step (d)  
(Abstract).

Favaloro et al. further teaches that type I vWD patients suffer from a quantitative reduction in all vWF multimers present, with concurrently decreased levels of vWF:Ag and ristocetin cofactor activity (p152, right column, *Introduction*, 2<sup>nd</sup> paragraph). Alternatively, type II vWD is characterized by qualitative abnormalities of vWF multimers (p152, right column, *Introduction*, 2<sup>nd</sup> paragraph). Classification of the patient's vWD is important not only because the biological activity of vWF is related to its multimeric profile, but also since subsequent clinical management of such patients may differ substantially on this basis (p152-3, *Introduction*, 2<sup>nd</sup> paragraph).

With respect to claim 41, Favaloro et al. teaches a method, wherein the sample is obtained from plasma of a patient (p152, right column, *Introduction*, lines 4-9).

With respect to claims 48 and 49, Favaloro et al. teaches a method, wherein detecting vWD under step e) comprises discriminating between type 1 and type 2 vWD (p153, left column, *Introduction*, lines 17-23).

However, Favaloro et al. fails to teach a detection step of a) uses a soluble form or a portion of glycoprotein 1b(α) (GP1b(α)) and ristocetin or a functionally equivalent substance.

Vischer et al. teaches vWF biology and pathology associated with vWD and its subtypes (see entire document). Type 2 vWD refers to qualitative deficiencies of vWF (p99, right column, 6.2 *Type 2 von Willebrand's disease*). Type 2 vWD is a heterogeneous category including subtypes 2A, 2B, 2M, and 2N (p99, right column, 6.2

*Type 2 von Willebrand's disease*). Type 2 is refers to qualitative deficiency of vWF (p99, right column, 6.2 *Type 2 von Willebrand's disease*). Type 2A is characterized by qualitative variants with decreased platelet-dependent function that is associated with the absence of high MW multimers and abnormal collagen binding often reflects a vWD type 2 variant (p103, left column, 7.2.2.2. *Collagen-binding assay for von Willebrand factor*). Type 2B is characterized by qualitative variants with increased affinity for platelet GP1b (p99, Table 2). The phenotype of type 2B can be detected by increased platelet agglutination at low concentrations of ristocetin (p100, left column, 6.2.2. *Type 2B von Willebrand's disease*).

Hoylaerts et al. teaches a method of detecting vWF activity in a sample (human plasma) using a soluble form or a portion of glycoprotein 1b (GP1b) and ristocetin (see entire document, particularly p454, *Purification of GPIb, Purification of vWF, and Studies of Interaction between vWF and GPIb*). Hoylaerts et al. teaches that the ristocetin-mediated vWF binding to immobilized GPIb is a reversible event (p457, right column, *Specificity of ristocetin-mediated vWF binding to GPIb*, lines 1-3). Therefore, coated GPIb is considered suitable for the study of ristocetin-dependent interactions between GPIb and vWF using an enzyme-linked immunoabsorbent assays (ELISA) format assay (p457, right column, *Specificity of ristocetin-mediated vWF binding to GPIb*, lines 4-6). To study this binding quantitatively, pure-GPIb-coated microtiter plates potentially offered an advantage over agglutination studies with formalin fixed platelets, in which ristocetin-mediated interactions with other platelet proteins participate (p457, right column, *Specificity of ristocetin-mediated vWF binding to GPIb*, lines 6-10).

Hoylaerts et al. further teaches that in order to avoid non-specific ristocetin-dependent molecular interactions, isolated GP1b was used instead of whole platelets (p462, left column, Discussion, 3<sup>rd</sup> paragraph).

With respect to claim 32, Hoylaerts et al. teaches a method of detecting vWF activity comprising detecting a formation of a complex of vWF and GP1b(α) (p p454, *Purification of GPIb, Purification of vWF, and Studies of Interaction between vWF and GPIb*).

With respect to claim 33, Hoylaerts et al. teaches a method of detecting vWF activity, wherein the method of detecting vWF activity, wherein is bound to a solid support (p454, left column, *Studies of Interaction between vWF and GPIb*, lines 2-5).

With respect to claim 35, Hoylaerts et al. teaches a method of detecting vWF activity, wherein the complex of vWF and GP1b(α) is bound to a solid support (p454, *Purification of GPIb, Purification of vWF, and Studies of Interaction between vWF and GPIb*).

With respect to claim 37, Hoylaerts et al. teaches a method of detecting vWF activity, wherein the detecting vWF activity under step a) comprises using an anti-vWF antibody (p454, right column, lines 30-33).

With respect to claims 38 and 39, Hoylaerts et al. teaches a method of detecting vWF activity under step a) comprising an ELISA (p454, right column, lines 30-33).

With respect to claim 52, Hoylaerts et al. teaches a method of detecting vWF activity, wherein the detecting vWF activity under step a) comprises using an anti-vWF antibody, which is detectably labeled (p454, right column, lines 30-33).

With respect to claim 56, Hoylaerts et al. teaches a method of detecting vWF activity, wherein the sample is diluted (p454, left column, *Studies of interaction between vWF and GPIb*, lines 5-7).

Handin teaches glycocalicin, which contains the majority of the extracellular portion of GP1b( $\alpha$ ) and can inhibit ristocetin-dependent binding of vWF (see entire document, particularly column 2, lines 51-68). Handin further teaches a method of obtaining human platelet GP1b( $\alpha$ ) receptor fragments containing the vWF binding site (column 3, lines 5-11) and antibody against the GP1b( $\alpha$ ) receptor fragment. Handin teaches that the antibodies and substantially purified antigen can be incorporated in a kit form such as ELISA (column 11, line 61-column 12, line 7), which involves immobilized antibodies either covalently or physically bound to a solid phase immunoabsorbent such as glass, polystyrene, polypropylene, dextran, nylon, and other materials in the form of tubes, beads, and microtiter plates (column 12, lines 47-61). Those skill in the art will appreciate that antibodies will be useful in other variations and forms of assays, which are presently known or may be developed in the future (column 12, lines 12-17).

With respect to claims 34 and 36, Handin teaches a method of immobilizing anti-GP1b( $\alpha$ ) antibody to a solid support (column 12, lines 47-61), which can be used in the detection assay for determining vWF activity, wherein a complex of vWF and GP1b( $\alpha$ ) is formed as taught by Hoylaerts et al. (p454, *Studies of interaction between vWF and GPIb*).

With respect to claim 40, Handin teaches a method of measuring vWF binding activity using a platelet aggregation assay (homogeneous agglutination assay, column 20, lines 59-68).

With respect to claim 50, Handin teaches a method of obtaining a recombinant human platelet GP1b( $\alpha$ ) receptor fragments containing the vWF binding site (column 3, lines 5-11).

With respect to claim 51, Handin teaches that the antibody against the GP1b( $\alpha$ ) receptor fragment is a monoclonal antibody (column 9, lines 43-44).

With respect to claim 53, Handin teaches a solid support, which is selected from a group consisting of glass, polystyrene, polypropylene, dextran, and nylon (column 12, lines 47-61).

With respect to claims 57-59, Handin teaches a method of immobilizing anti-GP1b( $\alpha$ ) antibody to a solid support (column 12, lines 47-61), which can be used in the detection assay for determining vWF activity, wherein a complex of vWF and GP1b( $\alpha$ ) is formed as taught by Hoylaerts et al. (p454, *Studies of interaction between vWF and GP1b*).

With respect to claim 60, Handin teaches a soluble form or a portion of GP1b( $\alpha$ ) containing an N-terminal domain of GP1b( $\alpha$ ) (column 2, line-column 3, line 2).

Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention to further employ the vWF binding activity detection method of Hoylaerts et al., in which a soluble form of GP1b is immobilized to detect ristocetin-mediated vWF binding activity, in addition to the collagen binding assay in the method

of Favaloro et al. in order to differentiate type 2B and type 2A vWD as Vischer et al. teaches that type 2A is characterized by qualitative variants with decreased platelet-dependent function that is associated with the absence of high MW multimers and Type 2B is characterized by qualitative variants with increased affinity for platelet GP1b. The advantage of further providing additional assay for measuring vWF binding activity for differentiating type 2A and type 2B vWD provides the motivation to combine teachings of Favaloro et al. and Hoylaerts et al. with a reasonable expectation of success as Vischer et al. teaches that variety of screening assays can be employed to further define the type of vWD (p102, Table 3). Further, it has long been held that it is obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose. *In re Kerkhoven*, 626 F.2d 846, 850, 205 USQ 1069, 1072 (CCPA 1980). In addition, it would have been obvious to one of ordinary skill in the art at the time of the invention to use a specific fragment of GP1b (extracellular fragment of GP1b(α)) as taught by Handin (soluble form) in the ELISA method of Hoylaerts et al. as the fragment of Handin contains ristocetin-dependent vWF binding site. One of ordinary skill in the art would recognize that the use of extracellular fragment of GP1b(α), which contains ristocetin-dependent vWF binding site, would be advantageous over the receptor complex GP1b of Hoylaerts et al., which contains components (such as GPIX) that are not involved in specific binding activity of vWF and increase likelihood of non-specific binding of vWF compared to the assay using extracellular fragment of GP1b(α).

11. Claims 54 is rejected under 35 U.S.C. 103(a) as being unpatentable over Favaloro et al. (*Pathology*, 1993, Vol. 25, pp152-158) in view of Vischer et al. (*Critical Reviews in Oncology/Hematology*, Apr. 1999, Vol. 30, pp93-109), Hoylaerts et al. (*Biochem. J.*, 1995, Vol. 386, pp453-463), and Handin (U.S. Patent No. 5,321,127, June 14, 1994) as applied to claims 31, 32, 35, and 53 above, and further in view of Batz et al. (U.S. Patent No. 4,415,700, Nov. 15, 1983).

Favaloro et al. in view of Vischer et al., Hoylaerts et al. and Handin teaches a method for detecting vWD as discussed above (see item 10 above). However, Favaloro et al. in view of Vischer et al., Hoylaerts et al. and Handin fails to teach a method, wherein the solid support comprises a latex bead.

Batz et al. teaches hydrophilic latex particles (beads), which can be used to covalently bind biologically and immunologically active substances either directly or via a coupling agent (see entire document, particularly Abstract). The hydrophilic latex particles of Batz et al. do not impair the structure and activity of the biologically and immunologically active substances, are stable under centrifuging conditions, can subsequently be resuspended again easily (column 2, line 59-column 3, line 2), and are especially useful for use in RIA, EIA, ELISA tests (column 5, lines 16-20).

Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention to use hydrophilic latex particles (beads) as a solid support having biologically and immunologically active substances as taught by Batz et al. in the ELISA test of Favaloro et al. in view of Vischer et al., Hoylaerts et al. and Handin for measuring binding activity of vWF since the advantage of hydrophilic latex particles providing a

solid support especially useful for ELISA tests without impairing the structure and activity biologically and immunologically active substances bound on the particles provides the motivation to combine teachings of Favaloro et al. in view of Vischer et al., Hoylaerts et al. and Handin and Batz et al. In addition, one of ordinary skill in the art would have had a reasonable expectation of success in combining teachings of Favaloro et al. in view of Vischer et al., Hoylaerts et al. and Handin and Batz et al. because the hydrophilic latex particles are especially useful in ELISA tests, which requires various incubation and washing steps of reagents and samples, since the particles are stable under centrifuging conditions and can subsequently be resuspended again easily.

12. Claims 55 is rejected under 35 U.S.C. 103(a) as being unpatentable over Favaloro et al. (*Pathology*, 1993, Vol. 25, pp152-158) in view of Vischer et al. (*Critical Reviews in Oncology/Hematology*, Apr. 1999, Vol. 30, pp93-109), Hoylaerts et al. (*Biochem. J.*, 1995, Vol. 386, pp453-463), and Handin (U.S. Patent No. 5,321,127, June 14, 1994) as applied to claims 31, 38, and 40 above, and further in view of Solen et al. (U.S. Patent No. 6,043,871, Filed Mar. 3, 1997).

Favaloro et al. in view of Vischer et al., Hoylaerts et al. and Handin teaches a method for detecting vWD as discussed above (see item 10 above). However, Favaloro et al. in view of Vischer et al., Hoylaerts et al. and Handin fails to teach a method, wherein the agglutination is measured by light scattering.

Solen et al. teaches a method of measuring platelet aggregation in whole blood in response to aggregating agents using light scattering detection method (see entire document, particularly Abstract). The instrument of Solen et al. is used in the clinical laboratory to evaluate the functional status of platelets in blood samples from patients suspected of abnormal platelet function (Abstract). The measurement is based on the scattering of light in the blood sample and does not require separation of erythrocytes from blood and therefore helps minimize the need for handling of blood by the laboratory personnel (Abstract). The instrument converts the light scattering data to provide the number and average size of the aggregates per unit volume at various times during the process of aggregation (Abstract).

Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention to use the detection instrument of Solen et al. utilizing a light scattering measurement in the agglutination method of Favaloro et al. in view of Vischer et al., Hoylaerts et al. and Handin because the light scattering measurement instrument of Solen et al. does not require separation of erythrocytes from blood and therefore helps minimize the need for handling of blood by the laboratory personnel. The advantage of not requiring further separation of erythrocytes from blood provides the motivation for combining teachings of Favaloro et al. in view of Vischer et al., Hoylaerts et al. and Handin and Solen et al. since elimination of further erythrocyte separation step would minimize the need for handling of blood by the laboratory personnel. Furthermore, one of ordinary skill in the art would have had a reasonable expectation of success in combining teachings of Favaloro et al. in view of Vischer et al., Hoylaerts et

al. and Handin and Solen et al. since the light scattering measurement instrument of Solen et al. provides quantitative analysis of platelet aggregation (agglutination) by measuring the number and average size of the aggregates per unit volume at various times during the process of aggregation.

13. Claim 61 is rejected under 35 U.S.C. 103(a) as being unpatentable over Favaloro et al. (*Pathology*, 1993, Vol. 25, pp152-158) in view of Vischer et al. (*Critical Reviews in Oncology/Hematology*, Apr. 1999, Vol. 30, pp93-109), Hoylaerts et al. (*Biochem. J.*, 1995, Vol. 386, pp453-463), and Handin (U.S. Patent No. 5,321,127, June 14, 1994) as applied to claim 31, and further in light of Vicente (*J. Biol. Chem.*, 1988, Vol. 263, pp18473-18479).

Favaloro et al. in view of Vischer et al., Hoylaerts et al., and Handin teaches a method for detecting vWD as discussed above (see item 10 above). Handin further teaches that glycocalicin, which contains the majority of the extracellular portion of the GP1b( $\alpha$ ) chain can be further digested to obtain an amino terminal 45 kDa fragment, which contain the vWF binding site (column 2, line-column 3, line 2). Although, Favaloro et al. in view of Vischer et al., Hoylaerts et al., and Handin is silent on disclosing that the soluble form or a portion of GP1b( $\alpha$ ) comprises amino acid residues His1-Val289 of GP1b( $\alpha$ ), Vicente teaches that 45 kDa fragment of GP1b( $\alpha$ ) contains amino acid residues extending between His1-Arg293 of GP1b( $\alpha$ ) (see entire document, particularly Abstract). Therefore, it would be apparent that Handin's 45 kDa fragment of

GP1b(α) would intrinsically include a portion of GP1b(α) comprising amino acid residues His1-Val289 of GP1b(α).

### ***Response to Arguments***

14. Applicant's arguments with respect to claims 31-41 and 48-62 have been considered but are moot in view of the new ground(s) of rejection.

### ***Conclusion***

15. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

- Fischer et al. (U.S. Patent No. 6,228,613) teaches that specific platelet agglutination reflects the ratio of ristocetin cofactor acitivity and vWF antigen content and indicates specific activity of multimers (see entire document, particularly column 5, lines 6-9).
- Murray et al. (Transfusion Medicine Reviews, 1996, Vol. X, pp93-110) teaches pathogenesis, classification, and management of vWD (see entire document).
- Tefferi et al. (Am. J. Med., 1997, Vol. 103, pp536-540) teaches occurrence, diagnosis, pathogenesis, and treatment of vWD (see entire document).
- Zieger et al. (*Thrombosis Research*, 1997, Vol. 87, pp57-64) teaches variant type 2M vWD (see entire document).

16. No claim is allowed.

17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Unsu Jung whose telephone number is 571-272-8506.

The examiner can normally be reached on M-F: 9-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on 571-272-0823. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Unsu Jung, Ph.D.  
Patent Examiner  
Art Unit 1641



LONG V. LE 05/11/07  
SUPERVISORY PATENT EXAMINER  
TECHNOLOGY CENTER 1600